

>> Prenatal Testing FAQs for Patients

What are chromosomes?

Chromosomes are tightly bundled packages of DNA, the molecule that carries our genetic information, and that is present in almost every cell in our bodies. Most people have 46 chromosomes in nearly every cell of their bodies, and the chromosomes exist in two sets; we inherit one set of 23 chromosomes from our mother and one set of 23 from our father. In this way, DNA is passed from parent to child and contributes to development and health.

Why do I need to know about chromosomes?

It may be important for you to know that some pregnancies carry too many or too few chromosomes, or have missing or extra pieces of chromosomes. Too much or too little genetic information can cause problems in growth or development of the fetus, and may result in birth defects, delay in development, learning problems, behavior issues or other health problems in a child. In certain pregnancies, the chance for a difference in the number or structure of chromosomes may be higher, such as pregnancies in women over 35 years of age, pregnancies identified to have ultrasound abnormalities, or pregnancies in families already known to have a member of the family with a chromosome change.

Is there a way to test for chromosome problems?

Yes. Traditionally, chromosome testing also called *karyotyping*, looks at the number and structure of chromosomes in a pregnancy or after birth to identify gains, losses or rearrangements of entire chromosomes or chromosomal pieces. More recently, a new technology called array-based comparative genomic hybridization (*array CGH*) has been shown to be useful to test chromosomes. Array CGH is sometimes referred to as *microarray* testing.

What is array CGH or microarray testing?

Microarray-based comparative genomic hybridization (array CGH) is a type of chromosome testing. This technology takes a closer look at important areas of our chromosomes to see if there are extra or missing DNA pieces that could cause birth defects, delays in development, or other medical or learning problems.

How is array CGH different from karyotyping?

Array CGH is a technology that evaluates chromosome structure for extra or missing pieces even closer than can be achieved by karyotyping. Array CGH can identify nearly all chromosome imbalances that karyotyping can, and can also detect smaller extra or missing chromosome pieces that will be missed by karyotyping. These smaller imbalances, often called *submicroscopic* imbalances because they cannot be seen through the microscope, can still cause birth defects, delays in development, and genetic syndromes.

What are the benefits of performing array CGH in pregnancy?

Array CGH provides a more comprehensive analysis of the structure of the chromosomes of the prenatal sample. Prenatal diagnosis of a specific chromosome gain or loss can provide additional information that may enable your doctors to manage your pregnancy better and also may enable you and your doctors to know what to expect after delivery. Some parents request array CGH because problems have arisen in their pregnancy, such as a non-reassuring maternal serum screen, abnormal ultrasound findings, or abnormal karyotype, and they want as much information as possible to make informed decisions. Other parents request array CGH so they can plan and prepare for a child with anticipated medical or health issues. Still other parents request array CGH to provide further reassurance that a chromosome problem does NOT exist in their pregnancy. And in fact, other parents learn about the benefits and limitations of array CGH and then choose NOT to have the test based on personal beliefs and preferences.

Who should consider having array CGH?

Array CGH testing should be considered for any pregnancy for which traditional karyotyping would be offered. Common reasons for performing karyotyping and array CGH include advanced maternal age, abnormal maternal blood test indicating an increased risk for a chromosome abnormality, previous child or pregnancy with a known chromosome abnormality, abnormal ultrasound findings, and previous miscarriages or stillbirth.

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If karyotyping is done and the chromosomes of my pregnancy are normal, why consider array CGH?

Even if karyotyping is normal, array CGH has the potential to find a chromosome gain or loss that was either missed or cannot be detected by traditional chromosome analysis. Thus, array CGH offers an enhanced evaluation of chromosomes, and combined with karyotyping, provides a more complete evaluation of chromosomes in pregnancy.

Are there different options for using array CGH in prenatal testing?

Yes, our laboratory offers two different array CGH options for prenatal testing: For most situations, the Signature PrenatalChip® and the SignatureChipWG™ (Whole Genome). A third option, the SignatureChipOS™ (Oligo Solutions) may be considered under special circumstances. You and your physician or genetic counselor can read more about these different microarrays in the document, *Prenatal Diagnosis Using Array CGH: A Guide to Microarray Testing*. We encourage you to discuss the benefits and limitations of each test thoroughly with your physician or genetic counselor to ensure that you are fully informed.

How do I know what array CGH option to choose for my pregnancy?

Your physician or genetic counselor can help you to decide which array CGH option is right for you and your pregnancy. In general, physicians, genetic counselors, and parents could consider the Signature PrenatalChip for pregnancies in which the indication for testing is advanced maternal age or parental anxiety. The SignatureChipWG could be considered for pregnancies in which the reason for testing is abnormal ultrasound findings, or an abnormal pregnancy karyotype. The decision about which microarray to request is personal and is based on thorough discussions with your health care provider about benefits and limitations of testing, medical findings in the pregnancy, and your family history and previous pregnancy history.

What type of sample is needed?

Array CGH is most commonly performed on cells that are obtained from a prenatal diagnosis procedure such as amniocentesis or chorionic villus sampling (CVS). Array CGH can also be performed on other types of samples, such as stored DNA, blood cells, or cells from a skin sample. Your doctor can help to determine which type of sample would be most appropriate to send for analysis. Also, we require that blood samples from both parents be submitted at the same time as the amniocentesis or CVS sample for complete interpretation of results.

Why do you need blood samples from both parents?

In some cases, a difference in chromosome structure is detected in the prenatal sample that has unclear clinical meaning. Not all changes in chromosome structure cause problems in a pregnancy or a person. Some changes run in families and do not cause any differences in health or learning. Other changes in chromosome structure cause birth defects or learning issues, the extent of which cannot be determined until after a child is born and begins to develop. When a change in chromosome structure is detected in a prenatal sample, blood samples from parents can be rapidly evaluated to get a more complete understanding of the clinical meaning. This can speed up the reporting of complete results without causing too much anxiety. As mentioned earlier, both the Signature PrenatalChip and the SignatureChipWG may find results with unclear clinical meaning, although it is expected to happen with lower frequency with the Signature PrenatalChip, a microarray specifically designed to minimize the likelihood of unclear results while maximizing the potential for detection of chromosome problems.

Is there a risk of miscarriage?

Array CGH itself does not pose a health risk to the fetus or the mother. However, karyotyping and microarray testing require a sample from the pregnancy, and the procedures performed to obtain the sample, such as amniocentesis or CVS have a risk of miscarriage associated with them. Your doctor or genetic counselor can talk to you about these risks and help you determine whether chromosome testing and microarray testing are appropriate for you.

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Can microarray testing find all chromosome differences?

No. There are some chromosome problems that microarray testing cannot detect, no matter what microarray is used. These include balanced chromosome rearrangements, in which pieces of chromosomes have broken and recombined in a balanced form, chromosome gains or losses that occur in areas not evaluated by the microarray, and some differences in the total number of chromosomes in the fetus. Karyotyping can find these types of chromosome differences, and for this reason, we recommend that karyotyping be performed prior to, concurrent to, or following microarray testing in pregnancy.

Can microarray testing find all genetic syndromes?

No. There are many causes of genetic syndromes, including but not limited to changes of the DNA sequence within genes (point mutations) or gains or losses of segments of DNA that are very small – too small to be detected by any microarray. Some of the genetic syndromes caused by chromosome gains or losses can ALSO be caused by point mutations or other types of genetic changes, and thus a normal array CGH does not exclude most genetic conditions.

When should I expect results, and who will contact me to discuss results?

In general, microarray testing takes 5-7 days from the time the sample is received by our laboratory. The results are reported by fax and mail to the ordering doctor. Your doctor, genetic counselor, or other designated health care provider will contact you to explain the results.

What does a positive or abnormal microarray result mean?

A positive or abnormal result means that a gain (duplication) or loss (deletion) in chromosome structure has been identified in the chromosomes of the pregnancy. Your doctor will explain the results to you.

What does a negative or normal microarray result mean?

A negative result means that microarray did not detect a gain or loss in chromosome structure. Many genetic conditions cannot be diagnosed by microarray testing, especially those that are caused by point mutations or other differences in DNA that are too small for even microarray to detect. Therefore a normal result cannot exclude all genetic conditions. Your doctor will discuss the results with you.

I have additional questions about microarray testing. Whom can I contact?

Your doctor, genetic counselor, or other genetics health care providers can talk with you more about the details of this testing. To find a genetic counselor, genetics clinic, or other genetics professionals in your area, please call your doctor, or our laboratory at 1.877.SigChip.

In accordance with Washington State Law RCW 7.70.050 and WAC 388-531-0050, providing patients with the information necessary for them to be able to give their informed consent for testing or treatment is the responsibility of the health care provider who has direct contact with the patient. Laboratory tests are ordered and prescribed by physicians so it is the physician, not the laboratory, that is required to obtain the patient's informed consent for testing.

The contents of the **Frequently Asked Questions for Physicians and Genetic Counselors, Frequently Asked Questions for Patients, Frequently Asked Questions for Prenatal Testing, and Prenatal Diagnosis and Array CGH: A Guide to Microarray Testing, and Physician Information Sheet for Microarrays in Prenatal Diagnosis** are provided for informational purposes only and are not and should not be construed as medical advice, diagnosis, or treatment. Only a properly qualified physician can address specific questions regarding a patient's health care needs. Individual inquiries about medical or healthcare issues should be addressed to appropriate healthcare professionals. Nothing contained in the **Frequently Asked Questions for Physicians and Genetic Counselors, Frequently Asked Questions for Patients, Frequently Asked Questions for Prenatal Testing, Prenatal Diagnosis and Array CGH: A Guide to Microarray Testing** or **Physician Information Sheet for Microarrays in Prenatal Diagnosis** should be used to replace or substitute for a patient's personal physician's advice.